REMARKS

Applicants have amended claims 1, 11, and 16 to recite the term "non-crosslinked" so as to more particularly point out and distinctly claim the subject matter of this invention. Support for the recitation can be found in the specification. Specifically, the specification provides an example (page 5, lines 12-25), in which unwound collagen monomers were allowed to randomly rewind in the absence of a crosslinking agent, heating, or radiation to form a substrate.[1] As a result, monomers merely rewound with each other via intermolecular interaction, such as hydrogen bonding or van der Warrs forces. Thus, "α-helical type I collagen monomers" recited in original claims 1, 11, and 16 are not crosslinked to each other. In other words, no new matter has been introduced by the amendments.

Applicants have also rewritten in independent form claims 7 and 10, which, according to the Examiner, cover allowable subject matter.

The amendments should be entered as they raise no new issues that will require further consideration or search and also do not touch the merits of the application within the meaning of 37 C.F.R. § 1.116(b).

Claims 1, 2, 6, 7, 9-12, 16, 17, 21, 23, and 24 are now pending. Reconsideration of the application, as amended, is requested in view of the remarks below.

Rejection under 35 U.S.C. § 103 (a)

The Examiner rejects claims 1, 2, 6, 9, 11, 12, 16, 17, and 21-24, asserting that they are rejected are unpatentable over Lai et al, U.S. Patent 5,876,444 ("Lai") in view of Muller et al., U.S. Patent 6,623,963 ("Muller") and Mansmann, U.S. Patent 6,530,956 ("Mansmann"). Claims 1, 11, and 16 are independent claims and will be discussed first.

Claim 1 covers a method of fabricating a cartilage implant. The method includes (1) embedding chondrocytes or mesenchymal stem cells in a three-dimensional substrate containing randomly rewound, **non-crosslinked** α-helical monomers from partially digested

[1] According to Lai et al, U.S. Patent 5,876,444 and Muller et al., U.S. Patent 6,623,963, crosslinking of type I or II collagen monomers requires a crosslinking agent, heating, or radiation.

type I collagen; and (2) growing the chondrocytes or mesenchymal stem cells in the substrate. Claim 11 covers a similar method but is limited to use of chondrocytes. Claim 16 covers a cartilage implant which contains (1) a three-dimensional substrate containing randomly rewound, **non-crosslinked** α-helical monomers from partially digested type I collagen, and (2) chondrocytes embedded in the matrix. The patentability of claims 1, 11, and 16 resides at least in part in use of **non-crosslinked** α-helical type I collagen monomers.

Lai discloses a method of preparing a reconstituted collagen template. The method includes (1) unwinding a triple-helical type I collagen to obtain α-helical monomers, (2) reducing residue disulfide bonds in the collagen to become -SH groups by mercaptoethanol, (3) **crosslinking** the α-helical monomers by utilizing glutaraldehyde, and (4) lyophilizing the cross-linked product to obtain the reconstituted collagen template. Clearly, the collagen template, corresponding to the substrate recited in claims 1, 11, and 16, is made of **crosslinked** type I collagen monomers. Specifically, the template is formed by crosslinking α-helical type I collagen monomers with glutaraldehyde. Glutaraldehyde is a straight alkyl chain having an aldehyde group at each of its two ends. In the cross-linking reaction, the two aldehyde groups respectively react with the side-chain amino group of an amino acid of one unwound type I collagen monomer and the side-chain amino group of an amino acid of another unwound type I collagen monomer.[2] As a result, two or more type I collagen monomers are crosslinked via covalent bonding. See column 4, lines 17-20 and Schemes III. Clearly, Lai does not teach or suggest use of **non-crosslinked** α-helical type I monomers, recited in claims 1, 11, and 16.

Neither Muller nor Mansmann cures this deficiency. Muller discloses an implantable article having a reconstituted type II collagen matrix, i.e., **crosslinked** type II collagen produced from non-crosslinked, atelocollagen form of type II collagen. See column 4, lines 47-50. Although, it also teaches a liquid or gel containing non-crosslinked type II collagen and cells, the liquid or gel is transformed into a **crosslinked** type II collagen matrix after it is injected into a site of a body simultaneously with a crosslinking agent. See column 6, lines 11-17. Mansmann discloses a scaffold, which may be made of unmodified collagen (e.g., type I collagen or type II

[2] Examples of amino acids having a side-chain amino group include asparagine, arginine, and glutamine.

collagen). See column 8, lines 35-48, and column 14, lines 28-43. Nowhere is mentioned in Mansmann unwinding collagen into monomers, let alone not cross-linking rewound collagen monomers.

As neither Muller nor Mansmann cures the deficiency of Lai, a combination of the three references does not teach or suggest use of non-crosslinked α-helical type I collagen monomers. In other words, contrary to the Examiner's assertion, claims 1, 11, and 16 are patentable over Lai in view of Muller and Mansmann.

Claims 2, 6, and 9 depend from claim 1, claim 12 depends from claim 11, and claims 17, 21, 23, and 24 depend from claim 16. For the same reasons set forth above, these claims are also patentable over Lai in view of Muller and Mansmann.

Objection

The Examiner indicated claims 7 and 10 each cover allowable subject matter, but are objected to as being dependent from a rejected claim. Applicants have rewritten them in independent form. It is submitted that amended claims 7 and 10 are now in condition for allowance.

CONCLUSION

Applicants submit that the grounds for rejection asserted by the Examiner have been overcome, and that claims 1, 2, 6, 7, 9-12, 16, 17, 21, 23, and 24, as pending, define subject matter that is nonobvious over the cited prior art references. Applicants ask that all claims be allowed.

Attorney's Docket No.: 10627-004001

Enclosed is a $55 check for the Petition for Extension of Time fee and an $86 check for claim fees. Please apply any other charges to deposit account 06-1050.

Respectfully submitted,

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